DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-661/S-024
NDA 20-460/S-010

Hoffman-LaRoche Inc.
Attention: Anthony Corrado
Program Director
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Mr. Corrado:

Please refer to your supplemental new drug applications dated August 27, 1999, received September 3, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cytovene-IV and Cytovene Tablets .

We acknowledge receipt of your submissions dated October 12, 2000.

The submissions, dated August 27, 1999 and the revised labeling supplement dated October 12, 2000 provide for changing the following under the **PRECAUTIONS** section, **Geriatric Use** subsection:

> "Clinical studies of CYTOVENE-IV and CYTOVENE did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy. CYTOVENE-IV and CYTOVENE are known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection. In addition, renal function should be monitored and dosage adjustments should be made accordingly. (see PRECAUTIONS: General: Renal Impairment and DOSAGE AND ADMINISTRATION)."

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted October 12, 2000).

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or

similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 19-661/S-024, 20-460/S-010." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Leslie Stephens, RN, MSN, Regulatory Project Manager, at 301-827-2335.

Sincerely,

Debra Birnkrant, M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research